

Docket No. 1385.45510X00 (P-3250)  
Serial No. 09/359,260  
Office Action dated October 31, 2005

### **AMENDMENTS TO THE CLAIMS**

The following listing of claims replaces all prior listings, and all prior versions, of claims in the application.

#### **LISTING OF CLAIMS:**

1. – 75. (cancelled)

76. (Previously presented) The method of claim 135, wherein said step of deriving a quantitative relationship comprises the step of determining  $y_i = f(x_{ij})$ , where  $x_{ij}$  denotes a whole molecule parameter,  $i$  ranges from 1 to  $n$  where  $n$  represents the number of first test peptides in the plurality thereof,  $j$  ranges from 1 to  $d$  where  $d$  represents the number of whole molecule parameters, and  $y_i$  represents an estimate of the measured indicia of the activity of the plurality of first test peptides.

77-81 (cancelled)

82. (Previously presented) The method of claim 135, wherein said space-filling design expands less than all of the first test peptides into their constituent compound isomers.

83 (Previously presented) The method of claim 135, wherein said first parameter is selected from the group consisting of total charge, molecular weight, isoelectric point and total dipole moment.

84. (Currently amended) The method of claim 135, wherein said first parameter is selected from the group consisting of total charge, molecular weight, isoelectric point and total dipole moment, and further wherein said ~~sequence-specific-second~~ parameter is selected from the group consisting of isotropic surface area, electronic charge index and hydrophobicity.

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85. (Previously presented)The method of claim 135, wherein said second parameter is selected from the group consisting of isotropic surface area, electronic charge index and hydrophobicity.

86. (Previously presented)The method of claim 135, wherein said first parameter is molecular weight and at least one additional parameter is selected from the group consisting of total charge, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, and hydrophobicity.

87. (Previously presented)The method of claim 135, wherein the activity is binding to a receptor.

88. (Previously presented)The method of claim 135, wherein the activity is enhancement or inducement of a biological activity in a cell.

89. (Previously presented)The method of claim 135, wherein the activity is inhibition or prevention of a biological activity in a cell.

90. (Original) The method of claim 88 or claim 89, wherein the cell is a cell cultured in vitro.

91. (Previously presented)The method of claim 90, wherein the step of measuring the indicia said activity comprises:

forming a plurality of culture media that each contains a respective test peptide from the plurality thereof; and

adding each of the plurality of culture media to a respective cell culture to form a plurality of cell cultures each containing a respective culture medium containing a respective first test compound.

92. (Previously presented)The method of claim 135, wherein the activity is inhibition or prevention of activation of a receptor.

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93. (Previously presented) The method of claim 135, wherein the activity is enhancement or inducement of activation of a receptor.

94. (Previously presented) The method of claim 135, wherein the first test peptide library consists of peptides having a length of no less than four amino acids.

95. (Previously presented) The method of claim 135, wherein the first test peptide library consists of peptides having a length of about four to about ten amino acids.

96. – 130. (Cancelled)

131. (Previously presented) The method of claim 137, wherein said step of performing a space-filling design is performed using a space-filling design that applies a distance function.

132. (Previously presented) The method of claim 137, wherein the number of initial peptides in said second test peptide library exceeds a predetermined threshold suited for performing said measuring step, and prior to conducting the step of measuring, performing the steps:

selecting a plurality of new peptides from said first test peptide library to form a new test peptide library using a space filling design;

deriving a new quantitative relationship between said measured indicia, said first parameter, and said second parameter;

calculating an estimated indicia for each initial peptide using said new determined relationship;

selecting a new second test peptide library comprising at least one initial peptide having an estimated indicia that satisfies said test requirement; and

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repeating said steps of selecting a plurality of new peptides, determining a new relationship, calculating an estimated indicia, and selecting a new second test peptide library until the number of initial peptides in said new second test peptide library does not exceed the predetermined threshold.

133. (Cancelled)

134. (Previously presented) The method of claim 137, wherein the number of initial peptides in said second test peptide library exceeds a predetermined threshold suited for performing said measuring step, and prior to conducting the step of measuring, performing the steps:

selecting a plurality of new peptides from said first test peptide library to form a new test peptide library using a space filling design;

deriving a new quantitative relationship between said measured indicia, said first parameter, and said second parameter;

calculating an estimated indicia for each initial peptide using said new determined relationship;

selecting a new second test peptide library comprising at least one initial peptide having an estimated indicia that satisfies said test requirement; and

repeating said steps of selecting a plurality of new peptides, determining a new relationship, calculating an estimated indicia, and selecting a new second test peptide library until the measured indicia of at least one of the initial peptides in the second test peptide library satisfies a predetermined threshold.

135. (Currently amended) A method of Identifying a peptide with a desired activity having an indicia that satisfies a test requirement, the method comprising the steps of:

identifying a predetermined set of peptides;

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parameterizing the predetermined set of peptides by:

determining a first parameter for each predetermined peptide, wherein the first parameter is a whole molecule parameter, and

determining a second parameter for each predetermined peptide, wherein the second parameter is dependent on the specific order of constitutive subunits within each predetermined peptide;

performing a space-filling design of the parameterized peptides to identify first test peptides;

constructing a first test peptide library comprising a plurality of first test peptides identified using the space-filling design, wherein the length of said first test peptides comprises about four amino acids to about twenty amino acids, and wherein said first test peptides are a subset of said predetermined set of peptides;

determining an activity, having an indicia, of said plurality of first test peptides;

measuring the indicia of said activity for said plurality of first test peptides;

deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter;

calculating an estimated indicia for each remaining peptide from said predetermined set of peptides using said quantitative relationship;

setting a test requirement, based on a desired activity, having a test indicia range;

selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide has an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

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measuring the indicia of each second test peptide; and

Identifying at least one second test peptide having a measured indicia that satisfies said test requirement.

136. (Currently amended) A method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement, the method comprising the steps of:

identifying a predetermined set of peptides;

parameterizing the predetermined set of peptides by:

determining a first parameter for each predetermined peptide, wherein the first parameter is a whole molecule parameter, and

determining a second parameter for each predetermined peptide, wherein the second parameter is dependent on the specific order of constitutive subunits within each predetermined peptide;

performing a space-filling design of the parameterized peptides to identify first test peptides;

constructing a first test peptide library comprising a plurality of first test peptides identified using the space-filling design, wherein the length of said first test peptides comprises about four amino acids to about twenty amino acids, and wherein said first test peptides are a subset of said predetermined set of peptides;

determining an activity, having an indicia, of said plurality of first test peptides;

measuring the indicia of said activity for said plurality of first test peptides;

deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter;

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setting a test requirement, based on a desired activity, having a test indicia range;

selecting a subgroup of first test peptides having an indicia that satisfies said test requirement; and

expanding first test peptides from said subgroup into their constituent compound isomers;

performing a space-filling design on said constituent compound isomers to identify candidate peptides;

calculating an estimated indicia for each candidate peptide using said quantitative relationship;

selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide is a candidate peptide having an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

measuring the indicia of each second test peptide; and

identifying at least one second test peptide having a measured indicia that satisfies said test requirement.

137. (Currently amended) A method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement, the method comprising the steps of:

Identifying a plurality of initial peptides having a length of about four amino acids to about twenty amino acids;

parameterizing the initial peptides by:

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determining a first parameter for each initial peptide, wherein the first parameter is a whole molecule parameter, and

determining a second parameter for each initial peptide, wherein the second parameter is dependent on the specific order of constitutive subunits within each initial peptide;

performing a space-filling design of the parameterized peptides to identify first test peptides;

constructing a first test peptide library comprising a plurality of test peptides identified using the space-filling design, wherein said first test peptides are a subset of said initial peptides;

measuring the indicia of an activity of said plurality of test peptides;

deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter of said plurality of test peptides;

calculating an estimated indicia for each initial peptide using said quantitative relationship;

setting a test requirement, based on a desired activity, said test requirement having a test indicia range;

selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide has an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

measuring the indicia of each second test peptide; and

identifying at least one second test peptide having a measured indicia that satisfies said test requirement.



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138. (Currently amended) A method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement, the method comprising the steps of:

identifying a predetermined set of peptides;

parameterizing the predetermined set of peptides by:

determining a first parameter for each predetermined peptide, wherein the first parameter is a whole molecule parameter, and

determining a second parameter for each predetermined peptide, wherein the second parameter is dependent on the specific order of constitutive subunits within each predetermined peptide;

performing a space-filling design of the parameterized peptides to identify first test peptides;

constructing a first test peptide library comprising a plurality of first test peptides identified using the space-filling design, wherein said first test peptides are a subset of said predetermined set of peptides;

determining an activity, having an indicia, of said plurality of first test peptides;

measuring the indicia of said activity for said plurality of first test peptides;

deriving a quantitative relationship between said indicia of said activity, said first parameter, and said second parameter;

calculating an estimated indicia for each remaining peptide from said predetermined set of peptides using said quantitative relationship;

setting a test requirement, based on a desired activity, having a test indicia range;

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selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide has an estimated indicia that satisfies said test requirement, and wherein said second test peptides are not in said first test peptide library;

measuring the indicia of each second test peptide; and

identifying at least one second test peptide having a measured indicia that satisfies said test requirement.